Avian Renal System: Clinical Implications

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KEYWORDS

• Avian • Renal • Diagnostics • Diseases • Treatments

Avian renal disease is common in veterinary practice.[1] However, it is often diagnosed during an advanced stage of disease. In the last few years, avian medicine has advanced in the recognition of kidney disease, but there is still a dearth of knowledge that needs to be rectified to better understand these diseases. This article serves as a guide to the current literature as well as some review topics pertinent to clinical avian renal disease.

ANATOMY AND PHYSIOLOGY

The avian renal system has anatomic and physiologic specificities that influence disease processes, diagnostics and treatment modalities. The kidneys are deeply imbedded within the renal fossae, the ventral depression of the synsacrum.[2] This is clinically relevant in cases of trauma and in the interpretation of imaging techniques. Nerves from the sacral and lumbar plexus pass through the kidneys.[2,3] Because of the close association with the kidney, any case of renal enlargement can cause nerve impingement, leading to paresis or paralysis. The kidneys account for approximately 1% of the bird's body weight.[2,3] They are symmetric and contain 3 lobes: cranial, middle, and caudal.[2] There are some species variations; for example, in passerines the middle and caudal lobes are fused.[2] In several species, such as herons, puffins, and penguins, the caudal lobe of the kidneys are fused at the midline.[2] Three main arteries supply each lobe of the kidney: the cranial, middle, and caudal renal artery, each supplying blood to its respective lobe.[2] The external iliac artery runs between the cranial and middle lobes, and the ischiadic artery runs between the middle and caudal lobes.

In birds, the most clinically significant renal anatomic feature is the renal portal system. The renal portal system is a ring of vasculature composed of cranial and caudal renal portal veins that branch off the left and right external iliac veins and left and right common iliac veins.[4,5] The renal portal system receives blood from the caudal mesenteric vein, the ischiatic vein, the internal vertebral venous sinus, and the internal iliac vein.[3] The renal portal system has a valve in the common iliac vein

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that is responsible for diverting blood away from or to the kidneys[4,5] The renal portal system is under adrenergic and cholinergic stimulation.[3] When the valve is closed as a result of stimulation by acetylcholine, blood is diverted straight to the kidneys and, when it is open as a result of stimulation by epinephrine, blood goes directly into the vena cava. This arrangement has clinical implications because blood from the caudal part of the body can travel directly to the kidneys. Although intramuscular injections in the legs are not routinely given in avian species, it is important to understand the function of the renal portal system, particularly when using potentially nephrotoxic drugs or drugs that may be cleared by the kidneys.

Avian kidneys differ from mammalian kidneys in that there is no defined cortex, medulla, or renal pelvis.[3] The avian kidney has 2 types of nephrons; the reptilian type and the mammalian type.[2] The mammalian type has cortical proximal and convoluted tubules and a loop with thin and thick segments descending into the medullary cones. The reptilian-type nephrons are smaller and more numerous, with only a short, poorly defined intermediate segment between the proximal and distal convoluted tubules with no loop of Henle.[3,5] The avian glomerulus has a similar structure and function to its mammalian counterpart.[6]

In the normal bird, most protein is excluded from the glomerular filtrate. The concentrations of glucose, amino acids, and electrolyte in the filtrate are the same as in plasma.[6] Glucose, most sodium, chloride, and amino acids are reabsorbed with water in the proximal convoluted tubule. The loop of Henle of the mammalian-type nephrons creates an osmotic gradient, resulting in an isotonic filtrate. In the distal convoluted tubules the filtrate becomes hypotonic as additional sodium is removed. This filtrate passes through the collecting ducts, which are impermeable to water, to produce hypotonic urine.[6]

The ureter starts at the cranial division of the kidney and courses caudally then branches to the middle and caudal renal lobes ending in the urodeum.[2] The ureter is lined by mucus-secreting pseudostratified epithelium that facilitates the excretion of urates in colloidal suspension.[2,4] The ureteral walls contain fibrous connective tissue and smooth muscle.[2]

Avian urine is stored in the urodeum where it can reflux back into the hindgut for water and electrolyte homeostasis.[4] In addition, in some species there is a supraorbital gland that contributes to water and electrolyte homeostasis.[4,7] This paired gland opens in the nasal cavity and responds to an increased plasma osmolality by secreting a watery fluid that is hyperosmotic to plasma.[4]

In mammals, the end product of protein metabolism is urea. Birds only produce small amounts of urea because they lack a functional urea cycle because of the absence of at least 2 of the essential enzymes.[3] In addition, most of the urea is completely excreted and is affected by hydration status.[8]

Uric acid is the predominant nitrogenous waste in birds and is produced mostly by the liver, with a small portion synthesized by the kidney.[3,9] Most of the uric acid is actively secreted by the proximal tubules.[2,4,10] Approximately 65% of the uric acid is protein bound.[5] In comparison with urea, which requires large quantities of water, uric acid can be excreted as a semisolid suspension with small amounts of water.[11]

Uric acid secretion is independent of water reabsorbtion, so it is minimally influenced by hydration status.[10] This is clinically significant because, as uric acid continues to be secreted, it cannot be flushed away from the ureter; this causes accumulation of uric acid within the tubules and possible ureteral obstruction (**Fig. 1**).

The avian kidney is also involved in regulation of water and electrolytes, production of vitamin D metabolites, excretion of metabolic wastes, and detoxification and secretion of endogenous and exogenous toxins.[3]

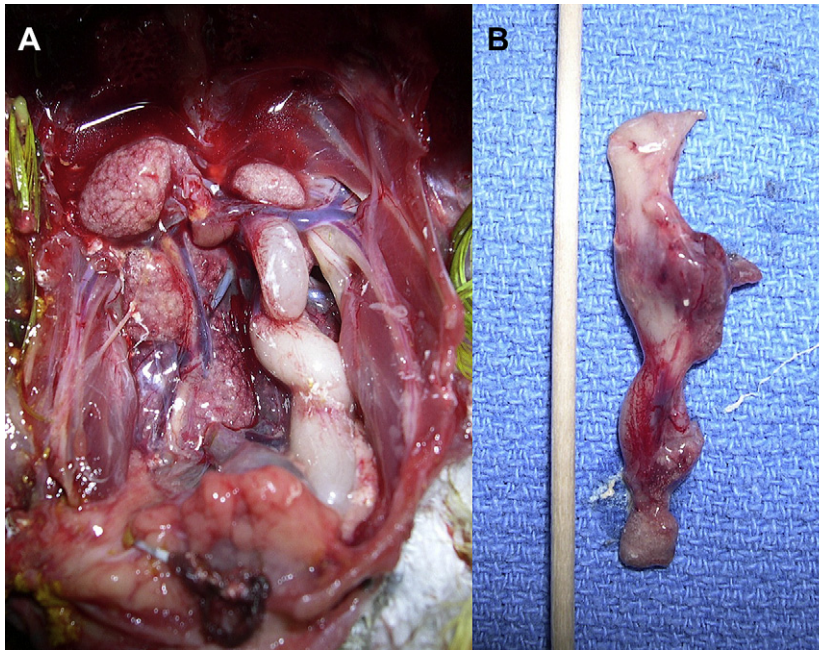

Fig. 1. (*A*) Severe dilation of the left ureter; note the atrophic left kidney and the enlarged right kidney, likely caused by a compensatory mechanism. (*B*) The ureter next to a cotton-tipped applicator to appreciate dilation.

CLINICAL SIGNS

In birds, clinical signs of renal disease are nonspecific. Possible signs include lethargy, weakness, crop stasis, vomiting, polyuria, polydipsia, lameness, muscle atrophy, deposition of urates in joints, feather-damaging behavior or self-mutilation over the synsacrum, and changes in urate character.[12–15] These signs can be present in a plethora of disease processes. For example, polyuria may not be of primary renal origin, and may be associated with diabetes, neoplasia, systemic infections, or other disease syndromes.[6]

RENAL INJURY

Renal injury in any species is a complex process and it is influenced by many factors. In mammals, an inflammatory cascade occurs during renal disease.[9] Although these same processes may not occur in the same manner in avian species, they may provide valuable insight into treatment modalities. During renal ischemia and vasoconstriction, prostaglandin and thromboxane production is increased.[9] This in turn causes changes in vascular resistance, blood flow, and recruitment of inflammatory cells. As a result of vasoconstriction and mesangial cell contraction and the effects of thromboxane A, a decreased glomerular filtration rate (GFR) can occur, leading to renal tubular damage from decreased oxygen and nutrient delivery.

DISEASES

There are several diseases that affect the avian renal system. These diseases can be of infectious origin (bacterial, viral, fungal, and parasitic) as well as noninfectious origin

(metabolic, nutritional, toxic, congenital). In a study in which 605 renal samples were submitted, 223 (37%) had renal lesions.[3]

INFECTIOUS CAUSES

Bacteria

Any bacterial organism associated with sepsis may be found in avian renal tissue.[1] In a retrospective study, 50% of nephritis cases were associated with bacterial disease.[4] Bacteria can gain access by an ascending infection from the cloaca to the ureter or via the hematogenous route.[2] Ascending infections have been reported in some birds with ulcerative cloacitis caused by a *Salmonella* infection.[3] In cases of colitis, infectious agents, toxins, and inflammatory products can gain access to the kidneys if blood draining from the colon is diverted into the renal vasculature.[9] It has been suggested that the renal portal system creates the potential for exposure of microbial or toxic agents from the alimentary tract to the kidneys.[4] *Staphylococci* and *Streptococci* have been reported as causative agents for renal disease in finches and canaries.[2] In pigeons, *Salmonella* infections have caused interstitial nephritis.[16,17] Enterobacteriaceae (*Escherichia coli*, *Klebsiella*, *Listeria*, *Yersenia*, and possibly *Proteus*) in chickens, *Erysipelothrix rhusiopathiae* in Coturnic quail and *Pasteurella* have also been implicated in renal disease.[2,3,9] *Mycobacterium* and *Chlamydophila* infections can cause pathology of the kidneys, but they usually cause systemic diseases.[2] There have been reports of *Chlamydophila* infection, but only affecting the kidneys in psittacines.[18] In 2 cases, the only organ that tested positive for *Chlamydophila* was the kidney, despite other organs being affected.

Viruses

Two of the viruses affecting the renal system are adenoviruses and polyomavirus, both causing renal enlargement.[2,3] Adenoviral infections are usually not clinically relevant and tend to be an incidental finding during histopathology.[3] In contrast, polyomavirus infection has been associated with clinical disease in passerines and psittacines.[2,3,6,15] In Gouldian finches, chronic renal disease with glomerular sclerosis is seen in those that survived acute polyomavirus infection.[2] Lesions such as interstitial nonsuppurative inflammation and mesangial cell necrosis may be seen in psittacine birds with avian polyomavirus disease.[2] As many of 70% of these birds will develop secondary glomerulopathy. This lesion is caused by the deposition of dense aggregates of immune complexes within the capillary lumen and the mesangium.[2] Ascites and anasarca have been reported in several species of parrots that are polymerase chain reaction (PCR)-positive for polyomavirus.[2] The ascites and anasarca are attributed to a protein-losing nephropathy or decreased hepatic production of albumin as a result of polyomavirus-induced hepatic necrosis.[2] Other viruses that can cause a nonsuppurative inflammation of the renal interstitium include reovirus, paramyxovirus, and West Nile virus.[2]

Fungi

Fungal infection affecting the kidneys is associated with extension of a fungal air sacculitis or systemic infection (fungal thrombosis).[2,6] The kidney is rarely involved in either case.[3] In 11 cases of systemic mycotic disease, 2 had renal involvement.[3] Both cases had renal infarction associated with thrombi containing fungal hyphae, suspected to be *Aspergillus* species. Large fungal granulomas can affect renal function as a result of a mass effect, but they can also locally invade the kidneys.[6] Unless the kidney is severely affected, renal function is not typically affected in fungal

infections.[6] If renal function is affected with a mycotic infection, the bird usually has other signs of severe fungal disease.[6] These signs can include weight loss, labored or open-mouth breathing, voice change, or decreased vocalizations.

Parasites

Parasitic infections affecting the kidneys are not usually found in pet birds. They are often found in waterfowl and marine species.[2,9] Renal coccidiosis is the most common avian renal parasite and has been associated with clinical disease in several species of waterfowl, such as ducks, graylag geese, and a loon.[2,9,19,20] The renal tubules are affected, and severe tubular destruction can occur as well as interstitial nephritis.[9] Systemic protozoan disease in zebra finches has also been reported.[21] *Cryptosporidium* is not a common parasite affecting the kidney in avian medicine, but sporadic cases have been reported.[22,23] *Encephalitozoon hellem* has been associated with nephritis in lovebirds and budgies.[2] *E hellem* has been involved in severe disease in immunocompromised patients. In a study of healthy lovebirds, 25% of birds sampled had spores for *E hellem*.[24] Lovebirds that were PCR-positive for psittacine beak and feather disease were 3 times more likely to shed microsporidian spores.[24]

Renal trematodes have been reported in species such as waterfowl, passerines, poultry, pigeons, barbets, and psittacines.[2,25,26] In 2 barbets, these parasites were not associated with clinical signs and were considered an incidental finding.[25] In 3 psittacine birds, (2 macaws and a white-eared parakeet), clinical signs were associated with *Paratanasia robusta* infection.[26] All 3 birds had enlarged kidneys with yellowish-brown discoloration and irregular cortical surface. Histology showed a granulomatous nephritis with adult worms present within the dilated tubules. Paratanasia infection requires the ingestion of a terrestrial snail, and the authors of the article believed that the *Paratanasia* infection of these birds was accidental, as snails are not normally part of the psittacine diet.[26]

NONINFECTIOUS CAUSES

Nutrition

Renal disease such as nephritis, renal calcification (**Fig. 2**), and gout resulting from nutritional problems in avian species have been associated with high calcium and vitamin D, low vitamin A, or high protein levels in the diet.[2,9,11,27,28]

In nestling and adult budgies, diets containing 0.7% or more of calcium caused metastatic mineralization of the kidney.[2] In 1 case of a salmon crested cockatoo in which the diet contained 20 times the recommended amount of vitamin D_3, metastatic calcification of the kidneys, lungs, and proventriculus was present.[12] Recommendation of 1000 IU per kilogram of food has been made for psittacine birds.[12] Nephrosis and nephritis were present in poultry fed diets high in protein and calcium, containing urea, or deficient in vitamin A.[27,28] Hypovitaminosis A may also lead to renal disease.[9] Vitamin A deficiency causes metaplastic changes of the ureters and collecting ducts as well as decreased secretions of mucus within the ureter.[2,10] These metaplastic changes and decreased mucus secretion can lead to ureteral obstruction.[2,10] In poultry, diets low in vitamin A can lead to renal disease. Renal lesions include dilation and impaction of the collecting ducts with cellular debris, inflammatory cells and urates, tubular degeneration, and necrosis.[29] In psittacine birds, some diets are mostly seed based. Because of the likely low vitamin A level present in seeds, a similar association between renal disease and hypovitaminosis A can be made in pet birds.

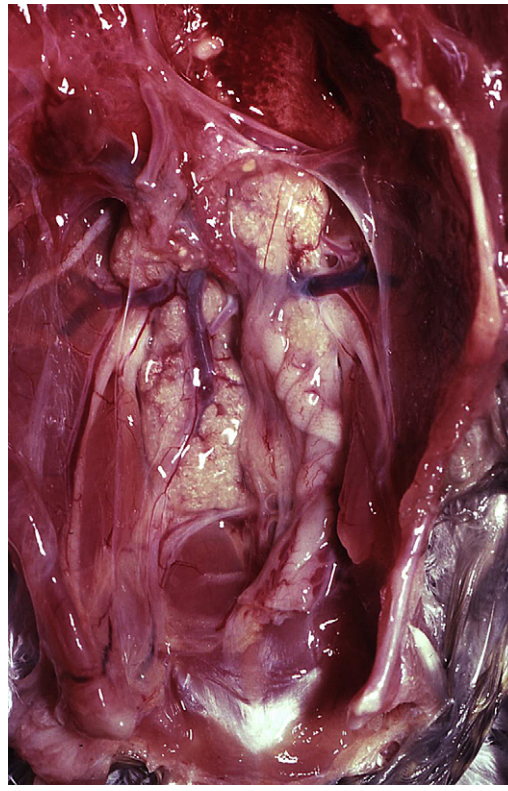

Fig. 2. Severe renal calcification in a cockatiel. (*Courtesy of* Drury Reavill, DVM, ABVP-Avian, ACVP).

Amyloidosis

Renal disease in avian species has been associated with amyloidosis.[9] Amyloidosis is not commonly seen in pet birds but is reported mostly in waterfowl, gulls, shorebirds, and small passerines.[2] Amyloidosis typically affects multiple organs and has been associated with end-stage renal disease.[2,9] It is usually associated with prolonged periods of stress and chronic inflammatory diseases.[30] In a flamingo that died with necrogranulomatous and septic air sacculitis hepatic capsulitis, and atherosclerosis, severe systemic amyloidosis was present. The amyloid deposit in the kidneys was severe and was considered to be the cause of death.[9] It has also been reported that pet geese have been presented with end-stage renal failure with renal amyloidosis.[9]

Lipidosis

Renal tubular lipid deposition has been reported in several avian species such as poultry, psittacines, and captive merlins.[2,15] It has been associated with high-fat or low-protein diets, starvation, biotin deficiency, and chronic liver disease.[2,15] Of clinical relevance in psittacine birds is the presence of chronic active hepatitis in Amazon parrots and cockatiels, which in turn can cause lipid deposition in the kidneys.[2] In pigeons fed diets supplemented with cholesterol, a high incidence of end-stage renal disease was seen compared with pigeons fed a control diet.[16] In psittacine birds this is

clinically relevant, because high-fat diets are commonly present and may affect the kidneys.

Myoglobinuric Nephrosis

Myoglobinuric nephrosis has been associated with exertional rhabomyolysis or severe crushing injury.[2] A similar presentation with anuric renal failure and increased uric acid levels has been reported in an ostrich.[3] Myoglobinuria has also been reported in a flamingo with capture myopathy.[15]

Gout

During dehydration there is decreased urine flow, leading to sludging of urate crystals within the tubules. If dehydration is transient, the lesion is reversible; persistent dehydration will result in renal failure.[2] In addition, dehydration can lead to decreased uric acid elimination. As uric acid levels increase in the blood and exceed the solubility of plasma, uric acid precipitation can occur, leading to gout.[2,9]

Two forms of gout occur in the avian species: visceral and articular gout.

Visceral gout occurs as a result of increased plasma uric acid levels, resulting in deposition of urates on various organs, particularly the pericardium, liver, spleen, and kidney (**Fig. 3**).[9,30]

Articular gout occurs when uric acid crystals accumulate within the synovial capsules and tendon sheaths of the joints.[9] In cases of articular gout, deposition of urates in the viscera typically does not occur.[29] Clinical signs include lameness, inability to ambulate, and swellings along the metatarsophalangeal and interphalangeal joints (**Fig. 4**).

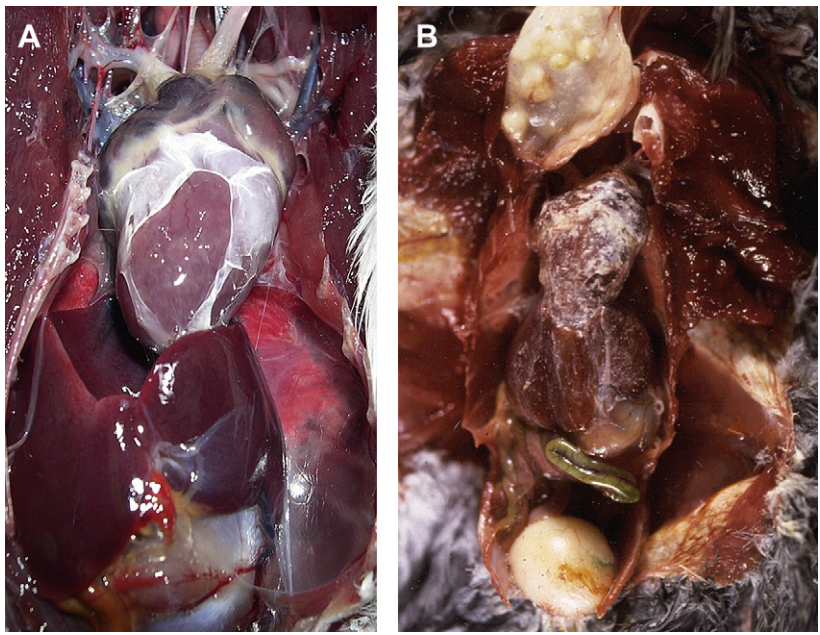

Fig. 3. (*A*) Visceral gout present in the pericardium. (*B*) Urate crystal deposit in the pericardium and hepatic surface. (*Courtesy of* Connie Orcutt, DVM, ABVP-Avian).

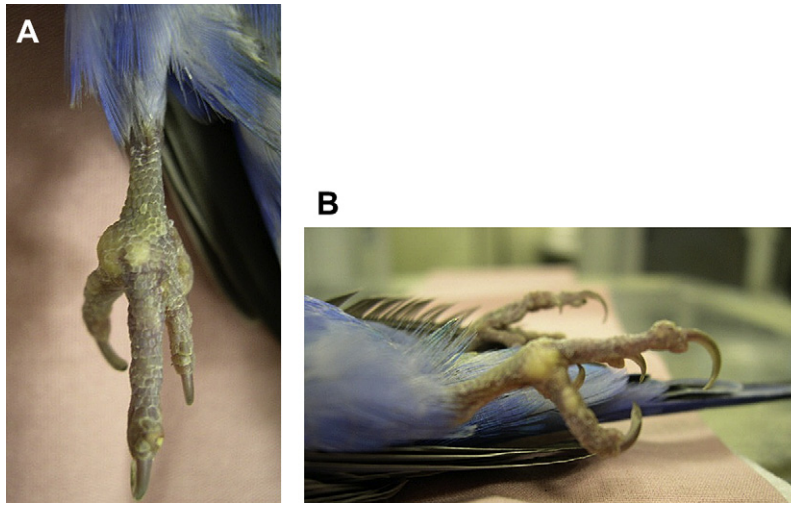

Fig. 4. (*A, B*) Articular gout present on metatarsus and interphalangeal joints.

Toxicity

In many cases, renal toxins cause similar gross and histologic lesions.[2] During the examination, a thorough history is needed to establish a list of potential toxins. The toxic substances affecting birds include rodenticides (vitamin D3 analog), aminoglycosides (gentamicin), lead, and zinc.[2] Renal nephrosis and acute tubular necrosis have been reported in avian species with lead and zinc toxicity.[31] This is clinically significant; this damage to the tubules can lead to further compromise of the patient because uric acid cannot be excreted appropriately, leading to potential uricemia. Calcium EDTA, one of the treatments for metal toxicity, has been associated with nephrotoxicosis in mammals. Calcium EDTA produces acute but reversible necrotizing nephrosis of the proximal convoluted tubules.[32] In birds of prey, calcium EDTA has been used in prolonged therapy (up to 23 days) with no deleterious effect.[33] However, no mention of histopatholgy to evaluate the kidneys of the birds of prey was mentioned. The author has also used calcium EDTA for prolonged treatment (3 weeks) with no clinical side effects in waterfowl and an African gray parrot.

Nephrotoxicity has been seen with the use of aminoglycosides in avian species.[34] In scarlet macaws and galahs, gentamicin administration for 7 days was associated with polyuria and polydipsia.[34] Renal tubule cells have an intrinsic ability to accumulate aminoglycosides via lumenal and basolateral transport in mammalian species.[35] It is presumed that this also occurs in birds but it has not been defined.

Nonsteroidal antiinflammatory drugs (NSAIDs) have the potential for nephrotoxicity in avian species.[36,37] Flunixin meglumine has been associated with nephrotoxicity in flamingos, cranes, and northern bobwhite quail.[38] Diclofenac, a new NSAID, was linked to a decrease in a population of vultures that ingested animals treated with this medication.[36] Acute renal necrosis and visceral gout was present in these birds. Similar histopathologic findings were present in pigeons, broiler chicks, Japanese quail, and mynah experimentally treated with diclofenac.[36] Mycotoxins such as ochratoxin and oosporein have also been associated with renal disease in avian species.[9] Oosporein toxicity has been associated with dehydration, stunted growth, nephromegaly, and death in chickens and turkeys.[9] Ochratoxin is produced by *Aspergillus* and *Penicillium* species that grow on moldy food, usually stored in high-moisture

conditions.[39] Oosporein is produced by *Chaetomium* sp and has been found in animal feeds, corn, and food products.[9,40] Although most of the reports have been in poultry, there is the potential for mycotoxins in pet birds because similar feeds, grains, and seeds are used in their diets, and these may be contaminated.

Neoplasia

Renal carcinoma and nephroblastoma are the most common tumors of the avian kidney (**Fig. 5**).[2,41] Other renal neoplasms include adenoma, cystadenoma, fibrosarcoma, and lymphosarcoma.[2]

Most commonly, clinical signs associated with renal tumors are abdominal distension and unilateral or bilateral lameness.[13,41] In a survey of 74 abdominal tumors in budgies, 63.5% were of renal origin.[41] An association with avian leukosis virus was investigated but the presence of antigen did not correlate with the presence or absence of tumors.[41] In 1 case of a cockatiel with a renal adenocarcinoma, osteopenia and muscle atrophy was noted in 1 of the limbs.[13] Prognosis for renal neoplasia is often poor because of the anatomic location of the kidneys, renal vasculature, and lack of response from chemotherapeutic agents.

Congenital Diseases

Congenital diseases occur in avian species but are often considered incidental findings. In a survey of poultry, one of the major defects involved the renal system.[42] Reported abnormalities were renal hypoplasia, dilated ureter, and remnant ureters.

Compensatory hypertrophy of the opposite kidney is generally present.[2]

Renal cysts can be solitary or multiple. This condition usually occurs as a result of incomplete fusion of the cortical portion of the tubule with ureteral tubules. In severe cases, this can lead to renal failure.[2] Glomerular hypervasculatiry, which has also been reported in a canary, leads glomerular deformation but does not result in immediate renal failure.[2]

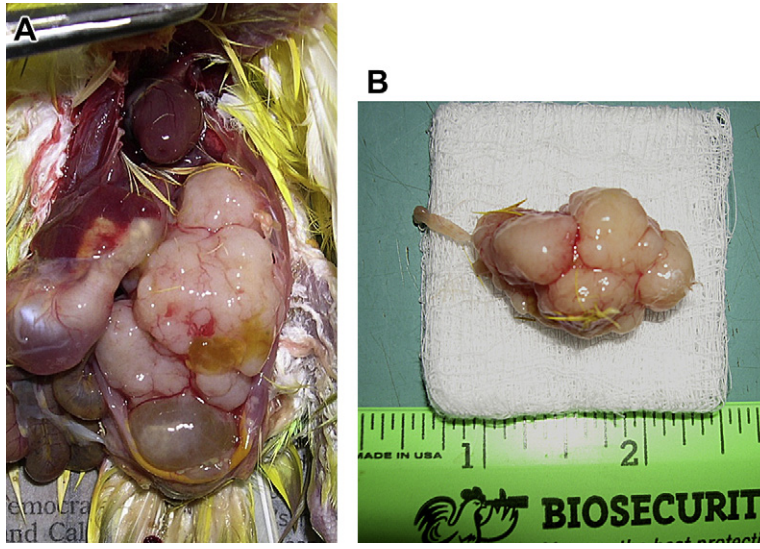

Fig. 5. (*A*) Renal adenocarcinoma on a budgerigar (*Melopsittacus undulatus*). (*B*) Mass after removal from the coelomic cavity.

Urolithiasis

Urolithiasis is a condition seen primarily in caged layer hens.[29] Lesions present within the kidney include tubular degeneration, renal atrophy, and enlargement and thickening of the ureter. The ureter contains accumulated mucus and ureteral stones. The cause of ureterolithiasis is unknown.[29] Possible causes may include water deprivation, excess calcium in the diet, viral infection, dietary/electrolyte imbalances, and hypovitaminosis A.[29,43]

Although not commonly seen in avian species, urolithiasis has been reported in a parrot and a penguin.[44,45] An ureterotomy was performed in an Amazon parrot with chronic ureteral stones.[44] Extracorporeal lithotripsy was performed in a Magellanic penguin (*Spheniscus magellanicus*) to remove renal stones.[45] In the case of the parrot, 2 ureteroliths were present and required multiple surgeries to remove them. This is partly a result of the complex anatomy of the avian renal system; because the kidneys are imbedded in the synsacrum, the ureter is closely adhered to the kidneys and the caudal aspect of the ureter is located in the dorsal aspect of the cloaca. The lithotripsy used in the penguin is a viable, noninvasive option to remove uroliths, because it uses shock waves to break up calculi, allowing the body to excrete them. One disadvantage is the need for specialized equipment to perform the procedure. As in any animal with urolithiasis, in addition to relieving any obstruction, treatment should include fluids, pain medications, and possibly antibiotics.

DIAGNOSTICS

Bloodwork

Renal function is determined in mammalian species by measuring glomerular filtration. GFR decreases in response to shock, blood loss, dehydration, glomerular or tubular disease, and postrenal obstruction.[6] Accurate determination of GFR requires measurement of clearance of exogenous (inulin) or endogenous compounds that are filtered through the kidneys within a 24-hour period.[6] In avian species, this is not a viable option because of the need for extensive anesthesia and cannulization of the ureter for extended periods of time to obtain urine that has not been contaminated with feces. For that reason, renal function is estimated by the measurement blood analytes such as uric acid, although other diagnostic tests may become available in the future.

Increased plasma uric acid only occurs when renal function is less than 30%, and can occur as a result of severe dehydration, damaged proximal tubules, obstruction, or congenital abnormality.[2,6,10] It only reflects the functional capacity of the renal tubules and is minimally affected by hydration status.[3] In 1 study with pigeons, high levels of plasma uric acid did not correlate with histopathologic changes in the kidneys.[46] The author has seen cases in which the uric acid has been within normal limits and, during postmortem examination and histopathology, the kidneys were severely affected.

Plasma uric acid levels have been shown to be increased after a meal in penguins, birds of prey, and broiler chickens.[47–49] It is therefore important to fast these species approximately 24 hours before blood sampling to get a more accurate value. In psittacines, studies conducted to evaluate changes in uric acid secondary to high-protein diets did not show a positive correlation.[50–52] Only cockatiels fed 70% protein in their diet had an increase in uric acid levels: no renal pathology was found in these birds.[52]

Urea has been used as an indicator for dehydration in birds.[10] Urea is produced in small amounts and is almost entirely excreted in the hydrated animal. In dehydrated pigeons, it has been shown that a large amount of urea is reabsorbed, thus suggesting urea as a potential indicator of dehydration in birds.[8]

Creatinine is excreted as creatine in the urine before its conversion, hence its clinical value is questionable.[5,10,46] Other parameters, such as protein, potassium, calcium, and phosphorus, have been used to aid in the diagnosis of renal disease in mammalian species. These values have not been consistent in the diagnosis of renal disease in birds, although changes in these values should be further investigated.

Urinalysis/Urate Character

Urinalysis is a valuable tool in general veterinary medicine. Urine dipsticks to assess renal disease are routinely used in mammals. In avian practice, urinalysis is not routinely performed.[10] One of its complications is the mixture of urine with fecal contents.[53] This makes the value of urine as a diagnostic tool debatable. A technique has been described to collect urine for urinalysis in pigeons, but this procedure can be time consuming.[54] In this procedure, the pigeon was fastened to a board and a cannula (cutoff 1-mL syringe without the plunger) was placed in the cloaca. Fecal matter from the cloaca was manually removed and periodic checks were performed to remove any feces. Four milliliters of urine were collected from the pigeons. In falcons, urine values for urinalysis were determined by aspirating and then centrifuging the urine portion from the droppings and then using the supernatant for analysis.[55] Birds may have polyuria as a stress response during examination; this may not represent the bird's eliminations at home (**Fig. 6**).[30]

Avian urine specific gravity is typically between 1.005 and 1.020 g/mL because of birds' decreased capacity for concentrating urine; only 10% to 30% of avian nephrons have loops of Henle.[6,7] The presence of abnormal specific gravity, cellular casts, proteinuria, glucosuria, ketonuria, or hematuria can have significant value.[10] Cellular casts in the urine may occur in diseased renal tubules.[30]

Urate color can indicate kidney disease, although other organ such as the liver may be involved. Normally, urates are white but, in presence of hepatic disease, biliverdinuria may occur, causing the urates to turn green or yellow.[6,30] This occurs because of the

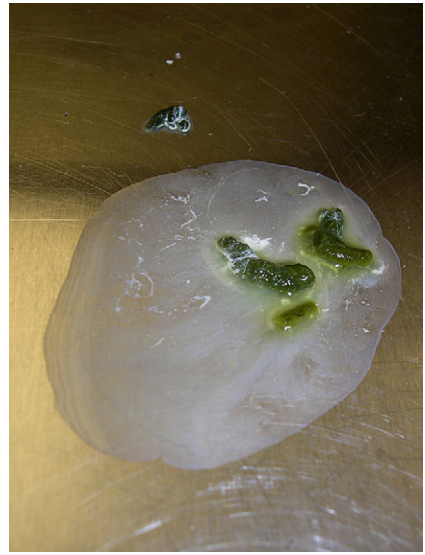

Fig. 6. Polyuria in an African gray parrot; likely stress related, because no evidence of renal disease was found in this bird. Note the excessive urine portion of the dropping.

accumulation of biliverdin, which is normally removed by the liver.[30] Unlike mammals, birds produce small amounts of bilirubin because of the decreased production of an enzyme (biliverdin reductase) that coverts biliverdin into bilirubin.[56] Hence, in a urinalysis, bilirubin should not be present.[6] Bile pigment nephrosis is a common finding in birds with liver disease.[6] Heavy metal toxicity in Amazon parrots causes hemoglobinuria, leading to a red or brown urate color.[6] Hematuria can be present from kidney disease or from cloacal, reproductive, or gastrointestinal origins (**Fig. 7**).[5,30]

Some clinicians have proposed using measurements of urine enzymes to help diagnose renal damage.[4,55] During renal damage, intracellular enzymes are not released into systemic circulation, but are present in the urine. The renal tissue in budgerigars and houbara bustards has high levels of lactate dehydrogenase, aspartate aminotransferase, creatine kinase, alkaline phosphatase, glutamate dehydrogenase, and alanine aminotransferase.[55] Determination of these enzymes may prove useful in the diagnosis of avian renal disease.

N-Acetyl-β-D-Glucosaminidase

N-Acetyl-β-D-glucosaminidase (NAG) is an exoglycolytic enzyme located in renal tubule lysosomes that has been used in mammals as a marker for renal damage.[57] This enzyme also exists in the avian kidney.[57] In pigeons, the kidney has the greatest NAG activity, although NAG is also present in the liver and intestines.[58] NAG is excreted during damage to the renal tubules (gentamicin, destruction of tubular epithelium, and increase in intracellular calcium concentrations in tubular cells). In hens, levels of NAG in the urine were increased after a 40-day supplementation of vitamin D 3.[57] In another study, pigeons that were given gentamicin had significantly increased urine NAG values compared with baseline.[58] In the hen study, timing of NAG measurement was suggested as a critical point in sample collection to provide a valid marker for kidney damage.[57] NAG values in the urine are normally higher in children and men, which may be of importance as normal avian values are developed.[58] Although further studies are needed regarding species variation, gender, and age, measuring urine NAG values may prove useful as a noninvasive measurement of renal disease in avian species.

Fig. 7. Hematuria present in an Eclectus parrot with lead toxicity. (*Courtesy of* Lauren Powers, DVM, ABVP-Avian).

Radiographs

The kidneys are located within the synsacral fossae, making it difficult to visualize them. Diverticula from the abdominal air sacs extend between the kidneys and the pelvis.[3] This is visible on a lateral view, and loss of this rim of air is interpreted as a sign of pathologic swelling of the kidney.[3] Increased renal opacity has been associated with dehydration or renal mineralization.[10] Renal tumors in the caudal division will displace coelomic organs in a cranial and ventral direction.[30] Tumors in the cranial and middle division will tend to displace the intestines caudally and ventrally and the ventriculus and liver cranially and ventrally. In some cases, urinary calculi are seen in the ureter (**Fig. 8**). Contrast studies of the gastrointestinal tract may help isolate the location of the kidneys.[5]

Ultrasound

Ultrasound studies to evaluate the kidneys are limited because of the presence of air sacs.[5,30] It does have applications in cases of suspected renomegaly, renal cysts, and ascites in which the kidney may be evaluated.[5] To perform an ultrasound in birds, a small head probe, 7.5-Mhz, 60-degree sector transducer should be used.[5] In some cases, a gel pad standoff may be needed, because the distance from the scanner to the target organ is short. Avian patients should be fasted for at least 3 hours to decrease food material within the gastrointestinal tract.

Advanced Imaging

Other imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT) scan, and nuclear scintigraphy have been used in avian species to evaluate the renal system, but these may not be readily available. Nuclear scintigraphy has been used to evaluate renal function in pigeons.[46] In this study, it was determined that technetium-99 dimercaptosuccinic acid (DMSA) can be better used to determine renal morphology, and that Tc 99m diethylenetriaminepentacetic acid (DTPA) should be used to evaluate renal function. Although valuable information can be obtained with this type of study, it does require a facility that routinely performs nuclear medicine procedures.

Renal Biopsy

To confirm renal disease antemortem, a renal biopsy is needed. Endoscopic-guided biopsy has been widely used in avian medicine. One of the main advantages of

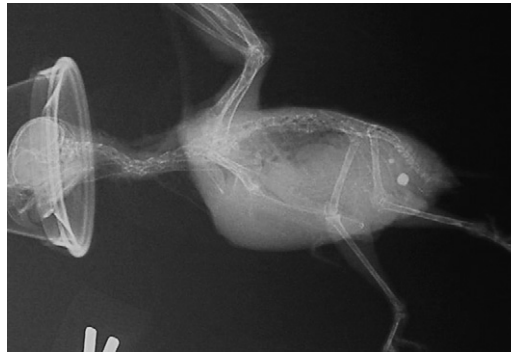

Fig. 8. Two urinary calculi in a psittacine.

endoscopic examination is the direct visualization of both kidneys as well as other coelomic organs.[4] Endoscopic examination of the kidneys is often recommended in cases in which there is persistent uric acid increase, polyuria, anuria, oliguria, and renomegaly on radiographic examination.

The endoscopic approach is usually into the left caudal thoracic air sac.[5] The limb can be retracted caudally or cranially.[59] The landmarks for the caudal technique are the last rib, the iliotibialis muscle, and the synsacrum.[5,59] In the cranial technique, the entry point is caudal to the pelvic limb and behind the last rib.[59] In birds of prey, an approach directly into the abdominal air sacs is not recommended because a large mass of tail muscles has to be penetrated, increasing the risk of bleeding.[4] The middle and caudal renal lobe are preferred kidney biopsy sites because the renal artery near the cranial lobe is more superficially located.[4,10]

A surgical biopsy technique to obtain kidney samples via a dorsal pelvic approach has been described.[60] An advantage of this procedure is that it requires minimal equipment. Also, iatrogenic trauma to the ureter, vas deferens, and caudal renal vein may be avoided.[60] Disadvantages include lack of visualization of other organs and the entire kidney, as with endoscopy. In addition, this procedure is more invasive than endoscopy.

Murexide Test

In cases in which articular gout is suspected, a small amount of aspirate from the suspected lesion is placed on a microscope slide and mixed with nitric acid. After allowing the mixture to dry over a flame, a drop of ammonia is added. If a mauve color develops, uric acid crystals are present.[4]

TREATMENT

Treatment of avian renal disease follows, for the most part, the treatment principles for mammalian renal disease. Because of anatomic and physiologic differences, it is difficult to achieve similar drug concentrations and durations between the 2 classes.[7] Allometric scaling has been used to help calculate drug dosages, taking into consideration the differences in anatomy, physiology, biochemistry, and pharmacokinetics in animals.[7] However, this equation has not been proven to be consistent, so it should be used with caution.[7,35] An overview of this topic has been published.[7]

Fluid Support

Different factors should be taken into consideration before fluid therapy administration, such as dehydration status, anorexia, and urine output. Once- to twice-daily weight measurements in critical patients may aid in determining fluid requirements.

In cases in which weight gain is not being achieved despite supportive care, hydration status must be assessed. Total fluid body requirement is about 4% of body weight in birds.[4] Maintenance fluid dosing for birds is typically 40–50 mL/kg/d.[9,15] Depending on hydration status and stability of the patient, several fluid routes are available. In cases in which the animal is stable and minimally dehydrated, subcutaneous fluids may be given. In more severe cases, intraosseous or intravenous fluids may be needed. Subcutaneous fluid administration is less invasive and does not require placement of catheters that the bird may remove. One major disadvantage is that the rate of absorption is much slower than intravenous or intraosseus fluid administration. Intravenous and intraosseus fluid administration has the advantage of more rapid fluid delivery to the patient, but thus requires the use of catheters that the bird may not tolerate. Caution should be taken to avoid fluid overload during fluid administration.

Antibiotics

As previously mentioned, 50% of avian nephritis cases have been associated with bacterial disease. For this reason, the use of antibiotics in renal disease should be strongly considered. It has been recommended that antibiotic administration should extend for 4 to 6 weeks in cases of bacterial renal disease.[9] Dosages for several antibiotics and other medications used in renal disease have been published.[61] Certain antibiotics should be used with caution, particularly aminoglycosides, in cases in which renal disease is suspected, because these are nephrotoxic.[2]

Nutrition

In cases of renal disease, the bird can also be malnourished or on a seed-based diet. In anorexic animals, hand-feeding formulae can be used to aid with nutrition, by providing essential nutrients needed for recovery. In cases in which hypovitaminosis A is suspected, supplementation of vitamin A should be implemented at a recommended dose of 2000 to 5000 IU/kg intramuscularly once a day for 2 weeks, followed by a lower dose of 1000 IU orally daily.[15] ω-3 fatty acids have been used as an adjunct therapy for renal disease because of their antiinflammatory, lipid-stabilizing, and renal-protective properties, among others.[9] Although no controlled studies in avian species exist regarding the use of ω-3 fatty acids, ω-3 fatty acids have been shown to reduce thromboxane A synthesis and increase production of vasodilatory prostaglandins in dogs.[62] In addition, fatty acid–supplemented dogs had a decreased tubular necrosis secondary to gentamicin administration, compared with control groups. Clinically, ω-3 fatty acids, alone or in combination with low-dose aspirin, have been used successfully in avian cases with confirmed glomerulopathy.[9]

The author has observed that a significant number of psittacine birds are on seed-based diets. These birds need to be gradually switched to a pellet-based diet supplemented with fresh fruits and vegetables. The author recommends that 50% of the diet be pellets, with 25% for fruits and vegetables, 15% for nuts, and 10% for seeds.

TREATMENT OF GOUT/HYPERURICEMIA

Overall, prognosis for gout tends to be poor, as treatment is usually not rewarding and clinical signs tend to interfere with quality of life. Several medications have been used in an attempt to reduce plasma uric acid levels. Surgery has been proposed to help remove the uric acid crystals in articular gout lesions.[9] This procedure is painful, so pain medications should be used. Medical treatments of hyperuricemia have included allopurinol, colchicines, and urate oxidase.[15]

Allopurinol

Allopurinol is a competitive xanthine oxidase inhibitor that blocks the metabolic pathways from hypoxanthine via xanthine to uric acid, thus decreasing uric acid production.[9,63] Allopurinol must be used with caution in birds of prey, because it has been shown that allopurinol increases uric acid levels and may lead to gout.[63] In a study with red-tailed hawks given allopurinol at doses of 50 mg/kg once a day, there was an increase of oxypurinol, a nephrotoxic metabolite of allopurinol, and xanthine, which is believed to reduce renal function.[63]

Urate Oxidase

Urate oxidase catalyzes the conversion of urate and oxygen into allantoin and hydrogen peroxide; allantoin might be further degraded to, and excreted as, allantoic

acid.[4] It has been studied in pigeons and red-tailed hawks and may be useful for the treatment of hyperuricemia.[8]

Colchicine

Colchicine has been used in humans to treat gout and has been used clinically in avian species.[9] Colchicine reduces uric acid levels by reversibly inhibiting xanthine dehydrogenase. A recommended dose of 0.0 to 0.04 mg/kg by mouth once or twice a day has been published.[15]

SUMMARY

Although renal disease is frequently diagnosed in avian species, it is often not recognized clinically until its advanced stage. In addition, because the clinical picture in many cases is often similar to other diseases, accurate diagnoses are further complicated. For these reasons, it is imperative to recognize early clinical signs of renal disease and use diagnostic tests to aid in the treatment regimen. Fluid therapy, nutritional support, vitamin A supplementation, ω-3 fatty acids, and broad-spectrum antibiotics are a good initial treatment plan while further diagnostics are performed. It is of utmost importance to address any nutritional deficit that the diet may have, particularly in psittacine birds.

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